

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/588,553	FREYSSINET ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	James L. Grun	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1.  This communication is responsive to communications filed 18 November 2002.
2.  The allowed claim(s) is/are 36, 44, 43, 37-40, 64, 65, and 41, renumbered as claims 1-10, respectively.
3.  The drawings filed on 07 June 2000 are accepted by the Examiner.
4.  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All    b)  Some\*    c)  None    of the:
    1.  Certified copies of the priority documents have been received.
    2.  Certified copies of the priority documents have been received in Application No. 08/750,776.
    3.  Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5.  A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6.  CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a)  including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1)  hereto or 2)  to Paper No./Mail Date \_\_\_\_\_.
  - (b)  including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7.  DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

#### Attachment(s)

1.  Notice of References Cited (PTO-892)
2.  Notice of Draftsperson's Patent Drawing Review (PTO-948)
3.  Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4.  Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5.  Notice of Informal Patent Application (PTO-152)
6.  Interview Summary (PTO-413),  
Paper No./Mail Date 08/03/2005.
7.  Examiner's Amendment/Comment
8.  Examiner's Statement of Reasons for Allowance
9.  Other \_\_\_\_\_.

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In view of the Appeal Brief and amendment filed 18 November 2002, PROSECUTION IS HEREBY REOPENED. As the amendment addresses issues discussed with Supervisory Patent Examiner Le and simplifies the issues for consideration, the amendment filed 18 November 2002 has been entered. Claims 36-44, 64, and 65 remain in the case after entry of the amendment.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Monica Chin Kitts on 03 August 2005.

The application has been amended as follows:

IN THE SPECIFICATION:

Page 1, in the insert before line 1 made by the Preliminary Amendment filed 07 June 2000, the paragraph beginning "This application..." was deleted and replaced with the following:

-- This application is a continuation application of U.S. Application Serial Number 08/750,776, filed December 19, 1996, now abandoned, the disclosure of which is hereby incorporated by reference, which is a 35 U.S.C. 371 filing of PCT/EP95/02846 filed July 19, 1995. --

IN THE CLAIMS:

The following listing of claims replaced all prior versions:

-- 36. (Currently amended) A method for determining a thrombotic or prethrombotic state, disease or risk therefor in ~~an individual being screened for screening for said state, disease and identification of~~ or risk factors, comprising:

obtaining a body fluid sample from the individual, said sample suspected of comprising a member selected from the group consisting of circulating microparticles, stimulated procoagulant cells and mixtures thereof;

incubating mixing the sample containing said member with a solid phase-bound purified receptor specific for a phospholipid, under conditions to form an immobilized complex on the solid phase of the purified receptor and any said member present in said sample; wherein said purified receptor is bound to a solid phase;

washing the incubated solid phase to remove removing unbound components; and determining any a level of prothrombinase activity of the washed immobilized complex, wherein an elevated level of prothrombinase activity determined for the immobilized complex compared with a level determined for normal body fluid samples indicates a thrombotic or prethrombotic state, disease, or elevated risk therefor in the individual bound to said solid phase; as an indication of an

individual's prethrombotic state; and

comparing the individual's prethrombotic state to prethrombotic values associated with an assortment of diseases and risk factors, thereby screening for disease and identifying risk factors.

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37. (Currently amended) The method according to claim 36, wherein prothrombinase activity of said complex is determined directly on said solid phase.

38. (Currently amended) The method according to claim 36, wherein prothrombinase activity of said complex is determined by determining prothrombinase activity of the bound said member after removing said bound member from said complex from said solid phase.

39. (Previously presented) The method according to claim 36, wherein said purified receptor is annexin V.

40. (Currently amended) The method according to claim 39, further comprising adding calcium ions in the incubating and determining steps when mixing said sample containing said member with the purified receptor specific for a phospholipid.

41. (Previously presented) The method according to claim 36, wherein said purified receptor is bound to the solid phase via a specific binding pair comprising a first and a second binding pair member, and wherein said first binding pair member is attached to the solid phase and said second binding pair member is coupled to said purified receptor.

42. (Cancelled).

43. (Currently amended) The method according to claim 36 42, wherein inhibitors of thrombin, Factor Xa or both thrombin and Factor Xa are present during the incubating step-(a).

44. (Currently amended) The method according to claim 36 42, wherein the activation of prothrombin to thrombin is detected prothrombinase activity of the complex is determined by reacting the bound said member of the complex with a reagent comprising factor V, factor Xa, prothrombin (factor II) and calcium-ions for a time sufficient for activation of prothrombin to thrombin (factor IIa), stopping the reaction by complexation of the calcium-ions, and determining amount of thrombin generated in said reaction by reacting the generated thrombin with its ability to hydrolyze a chromogenic substrate therefor and comparing with a standard curve.

64. (Previously presented) The method of claim 36, wherein said purified receptor is bound directly to the solid phase.

65. (Currently amended) The method according to claim 36, wherein said purified receptor is bound indirectly to a the solid phase. --

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James L. Grun, Ph.D.

August 3, 2005

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